CARDIOVASCULAR SYPHILIS*

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Our knowledge of the behavior of syphilis in the cardiovascular system has passed through interesting stages in its development. The first stage was that of discovery. To Morgagni, in 1761, goes the credit of clearly recognizing the relation between syphilis and aortic aneurysm. The next definite step was taken by Ricord in 1845, when he gave us the earliest description of syphilis of the heart. He described a gumma of the myocardium. Then our own Dr. Welch, in 1876, added to the picture that of syphilitic aortitis; and Döhle, in 1885, first made clear and insisted upon the relation between syphilis and lesions of the aorta. The final step in the stage of discovery was taken by Reuter, in 1906, when he demonstrated the treponema pallidum in the wall of the aorta in syphilitic aortitis.

The next stage in our knowledge is that in which the facts that had been obtained from postmortem material were applied to the diagnosis of syphilis of the heart in the living. This only began in 1906, after the discovery of the Wassermann reaction. Longcope[1], in 1913, painted a very clear picture of the diagnosis and treatment of syphilitic aortitis, and Brooks[2], in the same year, laid strong emphasis upon involvement of the myocardium, both in the secondary and tertiary stages of the disease. Warthin[3], in 1917, attracted further attention to the myocardial lesions of syphilis.

Now it is possible that we are entering upon a third stage in our knowledge of syphilis of the cardiovascular system. Syphilis has been fairly adequately treated for the past fifteen years. Much of the fundamental work has been done in the pathology and the clinical diagnosis of the condition. Nevertheless, we know very little about

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such important points as the time when aortitis begins to be manifest, the efficacy of early treatment in preventing cardiovascular involvement and the influence of treatment upon the course of the disease. With our recent development of the statistical method of study of large numbers of patients, over long periods of time, and with our highly developed system of follow-up, is it not possible that we are on the way toward providing an answer to many of these important questions in the natural history of the disease?

It is obviously not possible nor desirable to give, within the limits of this paper, a formal presentation of the entire subject of cardiovascular syphilis. Instead, an attempt will be made to paint a picture of the disease as a whole based upon the fundamental work that has been done in the past and, at the same time, to call attention again to the great gaps in our knowledge that make this picture incomplete. In the past, our thinking has been hampered by the habit of considering the various manifestations of syphilis of the cardiovascular system as separate disease entities. We have been drilled in the symptoms and signs of aneurysm, of aortitis, or of aortic insufficiency, and some of us have lost sight of the fact that they are only different manifestations of the development of the same pathologic process.

To begin at the beginning, in what manner does the spirochete reach the cardiovascular system? From the chancre, the organisms invade the blood stream and the lymphatics, pass through the right heart and into the lungs. Here those that do not pass through into the pulmonary veins and thence back into the heart and the general circulation are carried by the pulmonary lymphatics into the tracheo-bronchial lymph nodes. From here they are thought to pass by retrograde lymphatic flow into the tissues of the mediastinum and into the perivascular lymph spaces about the vasa vasorum in the adventitia of the aorta. Martland[4] has offered an ingenious explanation of the relative rarity of congenital syphilis of the heart and aorta. He has pointed out that in utero the pulmonary

circulation is small and that, therefore, only a small number of spirochetes are carried to the lung and thence to the tracheo-bronchial lymph nodes and aorta.

Now let us look for a moment at this matter of congenital syphilis. McCulloch[5] suggests that infants that are still born or die before aged two, correspond to the group of adults with generalized syphilitic invasion, the secondary stage. At postmortem, the myocardium shows evidence of syphilitic involvement with fibrosis and round cell infiltration. Spirochetes are often demonstrated, more frequently in the myocardium, but also in the aorta. The children that survive this period of invasion have either temporarily or permanently overcome their infection. Some of them, in later life, will develop syphilitic aortitis or myocardial gummata. Lamb[6] states that aortitis has been reported at ages twelve, seventeen and nineteen. On the other hand, careful clinical studies by Matusoff and White[7], McCulloch[5], Givan[8], Previtali[9], and others, have uniformly failed to show any demonstrable clinical signs of syphilitic heart disease in congenital syphilitics that survive. Is it not possible that in congenital syphilis, as in acquired syphilis, there is a long latent period from the time of infection to the onset of clinical signs and symptoms? To answer this very important question, we need more studies on older congenital syphilitics, and we need to keep them under observation, if possible, until death. To my knowledge, no such study has been made. Thus, to recapitulate, is it not possible that congenital syphilitics that are still born or that die during early infancy are in the period of invasion of the spirochetes which have come by way of the blood stream and invade the myocardium? If the individual survives, these organisms have been removed by phagocytosis, making myocardial lesions uncommon in those that outlive this period. The spirochetes that have been caught in the mediastinal lymph nodes, however, may reach the perivascular lymph spaces of the vasa vasorum in the aorta and initiate the lesions of aortitis. This condition we should expect to discover from fifteen to twenty years later.

Now let us turn our attention to some of the problems of the cardiovascular system in acquired syphilis. In this discussion, no attempt will be made to catalogue all the symptoms and physical signs of aortitis, aortic insufficiency and aneurysm, because they are too well known and have been ably recounted by others. Instead, let us think of syphilis of the cardiovascular system as a whole, and let us discuss some of its special problems. In the first place, why is it that the diagnosis is rarely made until twenty years after the primary lesion was acquired? Of course, one obvious explanation presents itself; the patient usually does not come for examination of the cardiovascular system until he is aware that something is amiss. Unfortunately, he does not reach this state until twenty years have elapsed since the chancre. It is generally agreed that infection of the heart and aorta takes place during the secondary stage of syphilis. The spirochetes probably lie inactive between the muscle bundles or in the perivascular lymph spaces and the vast majority are removed by phagocytosis. The remainder lie dormant for years, causing little or no tissue reaction. Fordyce[10] has suggested that allergy may offer an explanation for this phenomenon. The tissues may slowly become sensitized to the spirochetes so that, whereas in the beginning they did not react to the presence of these organisms, in the end, after several years, they react with edema, round cell infiltration and destruction of tissue, resulting in the development of recognizable clinical symptoms.

Some of the early writers have told us that a diagnosis of involvement of the heart can be made during the secondary stage of the disease. They point to palpitation, shortness of breath, tachycardia, bradycardia, premature beats and the development of apical systolic murmurs as evidence that this has occurred. They feel that the diagnosis is strengthened when these symptoms and signs clear up promptly under antiluetic treatment. More recently, workers who have studied cases of primary and secondary syphilis have failed to find definite evidence of involvement of the heart or aorta. The electrocardiogram and the x-ray

have shown no changes[11], and the symptoms and physical signs have been considered too indefinite to make a positive diagnosis. Clearly, the two views are diametrically opposed, and in order to arrive at a final conclusion, it will be necessary to study a large series of young syphilitics in the primary and secondary stages with all the means of cardiovascular examination at our disposal, and to employ very rigid criteria.

In the present state of our knowledge, what are the earliest recognizable symptoms of syphilitic heart disease? It will be remembered that the earliest lesions are in the arch of the aorta, above the semilunar valves. Aortic insufficiency, aneurysm and syphilitic coronary disease are late lesions. Therefore, we must try to diagnose syphilitic aortitis before these sequelæ have appeared. Lamb[6] found in his series of 26 cases of uncomplicated aortitis that eleven, or nearly half, had no symptoms whatsoever. Those that did have symptoms complained first either of substernal pain or paroxysmal dyspnea. The substernal pain was present most of the time but aggravated by exertion or emotion. He states that autopsy has shown that this symptom is not necessarily connected with changes in the coronary arteries.

White[12] states that aortitis itself may be symptomless, but that sometimes there is a more or less constant dull ache high up under the sternum. With our greater familiarity with the pain of coronary disease today, is it not possible that critical studies may be able to separate the early cases of aortitis from the more advanced, in which the mouths of the coronary arteries have become involved in the syphilitic process? Carter[13] calls attention to another early symptom; the abrupt onset of dyspnea on exertion, with slight edema. Thus, to help us in the early diagnosis of syphilitic aortitis, we have substernal distress or aching, paroxysmal dyspnea, often nocturnal, and the abrupt onset of shortness of breath on exertion. In addition, if we find a systolic murmur at the aortic area, a hollow ringing aortic second sound, in the absence of hypertension, evi-

dence in the teleoroentgenogram of a widened aorta, and a history of syphilis or a positive Wassermann reaction, the diagnosis of syphilis of the aorta has been made.

Now let us turn to the problem of syphilis of the myocardium. Gummata of the myocardium have been described since our earliest knowledge of syphilis of the heart. Their incidence is not very high but they are occasionally the cause of sudden and unexpected death. They are primarily vascular in origin, in that they begin as areas of round cell infiltration and necrosis about one of the branches of a coronary artery. True syphilitic myocarditis with diffuse infiltration of plasma cells between the muscle bundles, and parenchymatous degeneration of the muscle fibres, is a much rarer lesion, however. Warthin[14], in the course of his writings, has laid more and more stress upon chronic and acute syphilitic myocarditis. He states that the important, if not predominating, rôle played by syphilis in myocardial incompetency is not being recognized. His work, however, has not been confirmed by other careful students. It has, however, resulted in a tendency to overemphasize the myocardial lesions and thus distract attention from the aorta. Carter and Baker[13] found the myocardium alone involved in relatively few cases after gummata have been excluded. White [12] states that cardiovascular syphilis consists, therefore, primarily of luetic aortitis, infrequently it means myocardial disease. To recapitulate then, there is definite proof that myocardial gummata occur occasionally, but the existence of a true diffuse syphilitic myocarditis in acquired syphilis needs further postmortem proof.

Now what are the criteria for the diagnosis of syphilis of the myocardium? Given an unusual enlargement of the heart without demonstrable cause, a diffuse apex thrust without murmurs and with a poor first sound at the apex and a low systolic blood pressure in a patient with a positive Wassermann reaction and Carter[13] states that syphilitic involvement of the myocardium should be suspected. We

have seen one patient that fulfilled all these criteria and autopsy showed a large gumma in the myocardium.

Now before we discuss the treatment of cardiovascular syphilis, it is well for us to have in mind a clear picture of the morbid processes we are attempting to influence. In the first place, we know that the average duration of the disease from the chancre to the first diagnosis of cardiovascular syphilis is twenty years[15]. Again we know that the average period from the chancre to death is twenty-three years[15]. We remember the extensive changes that have taken place in the wall of the aorta, in an aneurysm, or in the aortic valves, in aortic insufficiency before a clinical diagnosis is usually made. Because of these facts, we approach the problem of treatment in true humility of spirit. When we begin treatment, the disease is already far advanced, and in spite of our best efforts, death comes on apace and the postmortem often shows a surprising amount of aortitis, in spite of so-called thorough treatment.

Gager[16] has recently called attention to some observations upon the comparative incidence of cardiovascular lesions in syphilis before and since the salvarsan era. Langer found syphilis in 4.02 per cent of necropsies in Virchow's Krankenhaus in 1906-07, and 4.32 per cent in 1925. However, the incidence of aortitis was 33.3 per cent in the first group before the salvarsan era and 83.87 per cent in 1925. Heller found that the number of aneurysms had quadrupled since salvarsan. Schlesinger showed that the time interval from the chancre to death was 23.4 years in untreated cases, 22.1 years in partially treated, and 15 years in the well treated. Whether these figures will be borne out by similar studies in this country remains to be seen. Nevertheless, they make us pause before we advocate vigorous antisyphilitic treatment for cardiovascular lues. The plans advocated by White[12], Carter[13], Lamb[6] and many others are similar in that they are all conservative and limit the use of neosalvarsan to small doses. It is agreed that antiluetic treatment should be omitted during periods of congestive failure and that when given, it should be in carefully plan-

ned courses with definite rest periods. The following plan is offered as one that has proven reasonably satisfactory in our hands. Treatment is begun with a course of mercury salicylate 0.03-0.06 gm. intramuscularly, once a week, for six weeks. At the same time, potassium iodide up to gms. 2, three times a day is given. Then a rest period of two months is allowed followed by a course of potassium bismuth tartrate 0.1-0.2 gm. intramuscularly until 2 gms. have been given, provided no toxic symptoms appear. After another rest period of two months, a course of six injections of neosalvarsan may be given, beginning with 0.1 gm. and increasing up to 0.45 gm. at weekly intervals. This plan of treatment will occupy about one year and should be continued for a second year and modified to suit the needs of the individual case. It is not often that one obtains a permanently negative Wassermann in these patients and, therefore, not the Wassermann reaction but the clinical condition of the patient should be the guide for treatment. The greatest danger is in overtreating these patients. If after a reasonable course of treatment they are doing well, they had best be left alone and kept under observation. It has been conclusively shown that the average duration of life from diagnosis of cardiovascular syphilis to death is from two to three years. A much larger series of carefully treated cases than have been reported so far is needed to show that this life expectancy can be increased. The hope for the future in the prevention of cardiovascular syphilis depends upon measures to prevent syphilis itself. Whether thorough treatment of the primary stages will prevent later involvement of the heart and aorta, it remains for further studies to show.

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